Opioid abuse

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Drug testing outside of the health care and criminal justice systems has increased throughout the past decade. Common situations where drug testing now occur include the workplace (pre-employment and random testing), the military, athletics events, and legal and criminal situations.[1] Misinterpretations of drug test results can have serious consequences, such as unjust termination of employment, risk of prison sentence, inappropriate exclusion from a sporting event, and possible medical mismanagement in emergency care settings. This mini review covers key aspects relating to the interpretation of opioid abuse.

Opioid: a naturally-occurring or synthetic substance that acts on one of the three main opioid receptors.

Calibrator: a solution that contains the analyte of concern at a known concentration.

Opioids belong to a class of drugs comprising both prescribed and illicit agents.[1] The term opioid describes a wide range of compounds, encompassing natural, semi-synthetic and fully synthetic opiates.[2] Morphine and codeine represent the naturally-occurring alkaloids in opium poppy seeds. Table 1 categorises opioid compounds according to the source of derivation.

Table 1: Classification of opioids[1]

Derivation	Opioid
Natural	Opium, morphine, codeine, thebaine
Semisynthetic	Heroin, hydrocodone, oxycodone, hydromorphone
Synthetic	Methadone, propoxyphene, fentanyl, meperidine

Opioids have varying therapeutic effects such as analgesic, antitussive and anti-diarrheal properties. Opioid therapy is well known for its pain relief in acute and chronic settings, with the hallmark being its ability to interact with the family of opioid receptors that are variably distributed throughout the body. Opioid receptor agonists typically produce analgesia whilst antagonists block this response.[2]

Opioids activate specific transmembrane neurotransmitters (mu, kappa and delta) located in the central and peripheral nervous systems. Activation of the mu receptors in the central nervous system results in responses such as respiratory depression, euphoria, analgesia and miosis, whilst stimulation of the peripheral mu receptors leads to cough suppression and opioid-induced constipation.[3]

Heroin

Heroin is a semisynthetic derivative of morphine. It is more potent than morphine and has a rapid onset of action. It can be injected, inhaled by snorting or sniffing, or smoked. It crosses into the brain where it is metabolised to morphine. Heroin produces a sense of euphoria accompanied by dry mouth, flushing of the skin and clouded mental functioning; whilst heroin overdose can lead to respiratory suppression which can be fatal.[4] Heroin is rapidly metabolised to 6-monoacetyl morphine (6-MAM), morphine and morphine glucuronide. 6-MAM is a product of heroin and not morphine

Table 2: Key aspects regarding heroin testing

Analyte	Onset of action	Metabolites	Specific metabolite	Detection window
Heroin	3-5 minutes	6-MAM, morphine and morphine glucuronide	6 monoacetyl lmorphine (6-MAM)	Morphine can be detected 2-4 days after use
6-MAM assay	Half-life: 36 minutes			8 hours

Table 3: Key analytical aspects regarding opioid/opiate testing

Analyte	Calibrator	DHHS cut-off level*	False positives	Confirmatory method/s
Opioids/Opiates	Morphine	2000 ng/ml*	Rifampicin	LC-MS/MS GC-MS
		Quinine		
		Quinolones		
		Dextromethorphan		

*Cut off defined by the DHHS (Department of Health and Human Services) in the workplace.[1]
LC-MS/MS: liquid chromatography mass spectrometry
GC-MS: gas chromatography mass spectrometry

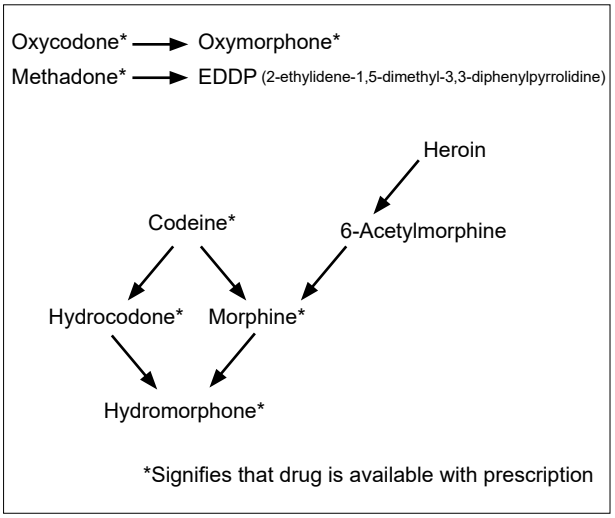

Figure 1: Metabolites of heroin, morphine and codeine (most common narcotic analgesics)[6]

or codeine, which makes it ideal for confirmatory testing. Unfortunately, this assay is not available in all laboratories, has a short half-life of 36 minutes, and is detected in the urine for up to only 8 hours after use.[1] Table 2 highlights key aspects regarding testing for heroin use.

Analytical testing for opioids

Urine is the preferred specimen for opioid testing due to its extended drug detection window and the non-invasive nature of the test.[5] Initial drug screening in most laboratories involves the use of immunoassays. In certain cases, screening results are followed by confirmatory testing using more sensitive and specific methods such as mass spectrometric methods linked to either ultra-high performance liquid chromatography (LC-MS/MS) or gas chromatography (GC-MS). Immunoassay-based drug screens are frequently used as they are rapid, inexpensive and can be automated. In the case of opioid screening, antibodies are directed against the common metabolite of heroin and codeine, namely morphine (Figure 1). Fentanyl, the synthetic opioid, is not detected by urine immunoassay testing as no metabolites are produced, thus giving a false negative result; whilst codeine is extensively metabolised, with 10-15% of the dose converted to morphine and norcodeine. It is clear that not all drugs within a class will cross react in assays, or may do so only at high concentrations. Many immunoassay platforms report a positive result only when values are above a defined threshold, e.g. 2000 ng/mL. The finding of a negative result, therefore, does not imply that the drug is not present. Another major concern associated with immunoassays is false positives due to cross reactivity. Antibodies in the assay may have limited specificity for the targeted drug or drug class and may exhibit cross reactivity to other closely-related compounds.[5] Some causes of these false positives include: rifampicin, poppy seeds, quinine, quinolones and dextromethorphan. Table 3 summarises key analytical aspects regarding opioid/opiate testing.

Conclusion

Given the complexities of drug testing and the importance of results for clinical decision making, it is imperative that clinicians understand the strengths and limitations of testing platforms. The laboratory can assist clinicians in this regard, ensuring that optimal care is achieved.

References

1. Moeller KE, Lee KC, Kissack JC. Urine drug screening: practical guide for clinicians. Mayo Clin Proc. 2008; 83(1):66-76.
2. Burtis CA, Ashwood ER, Bruns DE. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 5th Edition. St Louis: Elsevier; 2012.
3. Strain E, Saxon AJ, Hermann R. Opiod use disorder: Epidemiology, pharmacology, clinical manifestations, course screening, assessment, and diagnosis. UpToDate, 2015. Available at: http://www.uptodate.com/contents/opioid-use-disorder-epidemiology-pharmacology-clinical-manifestations-course-screening-assessment-and-diagnosis (accessed 21 Mar 2016).
4. National Institute of Drug Abuse (NIDA). Drug Facts. April 2013. Available at: http://atforum.com/documents/HeroinDrugFacts.pdf (accessed 24 Mar 2016).
5. Snyder ML, Melanson SEF. Drug addiction or false conviction. Clin Chem. 2014; 60(12):1480-1485.
6. Foley KF. Monitoring patient urine in the practice of pain management. Clinical laboratory. No.1, 2013. Available at: http://www.elearn.ascp.org/AngelUploads/Content/LQCL1301/_assoc/CL_13-01.html# (accessed 24 Mar 2016).